

G-quartet biomolecular nanowires

A. Calzolari, R. Di Felice, and E. Molinari

INFM and Dipartimento di Fisica, Università di Modena e Reggio Emilia,

Via Campi 213/A, 41100 Modena, Italy

A. Garbesi

CNR ISOF, Area della Ricerca, Via P. Gobetti 101, 40129 Bologna, Italy

Abstract

We present a first-principle investigation of quadruple helix nanowires, consisting of stacked planar hydrogen-bonded guanine tetramers. Our results show that long wires form and are stable in potassium-rich conditions. We present their electronic bandstructure and discuss the interpretation in terms of effective wide-bandgap semiconductors. The microscopic structural and electronic properties of the guanine quadruple helices make them suitable candidates for molecular nanoelectronics.

PACS numbers: 71.15.Pd, 71.24.+q, 87.15.Aa

Guanine (G) supramolecular systems receive great attention because of their peculiar structural and electronic properties: G molecules have the capability of forming a variety of self-assembled structures (helices, ribbons, tubes), both in solution and in the solid state [1, 2], and G-rich DNA sequences exhibit efficient long-range electron transfer properties [3]. Among the different G aggregates, in this letter we focus on tubular sequences of G-quartets [1], whose formation is driven by the presence of alkali cations: such tubes are often labeled as *G-quadruplexes* or *G-wires* [4]. The building block of a tube is the tetrameric G-quartet (G4) [1], which is a planar aggregate of four hydrogen-bonded guanines arranged in a square-like configuration, as shown in Figure 1a. Each G4 contains four carbonyl oxygen atoms pointing towards the center of the square. By stacking on top of each other, these tetramers form a tube-like column with a central cavity, that easily accomodates monovalent cations. X-ray and Nuclear Magnetic Resonance (NMR) data of both hydrophylic and lipophylic *G-quadruplexes* reveal that one cation is symmetrically located between any two G4 planes (Figure 1b), and coordinated with eight nearest-neighbor O atoms [5, 6]. G4 stacks exhibit a surprisingly high stability in different chemical conditions [1, 5, 6].

Besides the biochemical aspects [1], G-rich systems are attracting increasing interest in applied physics as functional elements in molecular electronics [7]. For example, guanine aggregates have been used to devise new conducting nanoscale materials, whose electronic features are typical of wide-gap semiconductors [8, 9]. Whereas recognition is a fingerprint of all the nucleic acid bases, guanine plays a key role to enhance charge migration [3, 10], because of its low ionization potential, and is suitable for electronic applications.

In this letter, we present a first-principle investigation of the structural and electronic properties of extended *G-wires*, free-standing or intercalated by K^+ ions. Our results show that in K-rich conditions G4 helices are thermodynamically stable, consistently with X-ray and NMR experiments [5, 6]. Although the single-particle bandstructure identifies the localized character of the electron wavefunctions, the calculated density of states (DOS) is consistent with a model of a semiconducting nanowire, which hosts extended channels for electron/hole motion. The peaks in the effective band-like DOS result from the energy spreading of the single-molecule energy levels. To our knowledge, this is the first theoretical prediction of the electronic properties of the extended tubular *G-wires*.

We performed first-principle total-energy calculations based on a Car-Parrinello-like scheme [12], with all the atoms free to relax towards the minimum energy configuration.

The electronic structure is described in the frame of plane-wave pseudopotential DFT [13], using the BLYP [14] exchange-correlation functional: this scheme gives a correct description of H-bonding in molecular systems [15]. The accuracy of the computational technique was tested on isolated G molecules and on self-assembled G-ribbons [11]. The *quadruplexes* are simulated by the use of periodically repeated supercells ($24.3 \times 24.3 \times 10.1 \text{ \AA}^3$), containing three stacked C_4 -symmetric G4 tetramers (Figure 1b), separated by 3.4 \AA and rotated by 30° (Figure 1c) along the stacking direction. The starting atomic configuration in our simulations was that resulting from the X-ray analysis of the G-*quadruplex* d(TG₄T) [5]. Neighboring replicas of the basic structural unit are laterally separated by vacuum, while a continuous wire is formed with its axis perpendicular to the tetrameric planes. Theoretical studies showed that the external backbone in helical nucleotide structures is not involved in transport phenomena [16]. Thus, we believe that our calculations for the G4 stacks are well representative of principal electronic features of real systems.

We studied two different G4 columns: the tube containing K^+ ions along the axis in the inner cavity is labeled 3G4/ K^+ [17], the empty tube is labeled 3G4. The formation energy E^{form} of each system, relative to that of isolated G molecules, as a function of the Fermi level (E_F) and of the chemical potential of K (μ^K), may be calculated after a thermodynamic approach successful for the study of defects in semiconductors [18], as

$$\Delta E^{form} = \Delta E^{tot} - \Delta n^K \mu^K - \Delta n^e E_F.$$

E^{tot} is the calculated total energy, n^K is the number of K atoms, n^e is the number of excess electrons with respect to charge neutrality: for 3G4 (3G4/ K^+) $\Delta n^K = \Delta n^e = 0$ ($\Delta n^K = +3$, $\Delta n^e = -3$). In the formula, μ^K and E_F depend on the conditions under which the material is formed and must be determined on the basis of physical constraints. To obtain Figure 1d, we assumed $\mu^K = \mu_{bulk}^K$, equivalent to fixing K-rich conditions. Under this assumption, the relative formation energy is a linear function of the Fermi level, and its slope is determined by the charge state Δn^e . Figure 1d shows the relative formation energy of the isolated G molecules, the 3G4 and the 3G4/ K^+ wires, as a function of E_F : for a given value of E_F , the lowest energy curve identifies the most favorable phase. The plot reveals that the G columns are energetically favorable with respect to isolated guanine molecules, due to the stability effect of the several hydrogen bonds. The 3G4/ K^+ structure is more stable than the 3G4 structure for E_F less than 1 eV: the energy gain is 1.8 eV/G4 for $E_F=0$. As we discuss

in the following paragraph, the G-wires exhibit an energy bandgap between the HOMO and the LUMO, and the condition $E_F=0$ corresponds to pinning the Fermi level at the top of the occupied energy levels. This condition is consistent with the abundance of metal cations, that may act as electron acceptors. Under these circumstances, the high stability of the K^+ -containing columnar structures is in agreement with the experimental evidence that the *quadruplexes* form only in the presence of metal cations [1, 5, 6]. We find that the empty 3G4 tube is unfavorable with respect to isolated G4 tetramers by 1.4 eV/G4, and the inclusion of K^+ ions stabilizes the columnar phase also with respect to the free tetramers. We attribute this effect to electrostatic K^+-O^- interactions that counterbalance the strong K^+-K^+ repulsion [19]. A K^+ concentration smaller than 1/G4 would break this equilibrium and would not be sufficient to induce the formation of the G-wires. Our results agree with cluster quantum-chemistry calculations [20].

The electronic bandstructure of the 3G4/ K^+ tube is shown in the right panel of Figure 2, while the left panel illustrates the DOS of both the K^+ -filled (bottom) and the empty (top) tubes. For other G stacks [11], π - π coupling may give rise to delocalized Bloch-type orbitals, whose band dispersion depends on the relative rotation angle between nucleobases in adjacent planes. In the guanine *quadruplexes*, the C_4 symmetry increases the spatial π - π overlap with respect to a segment of G-rich B-DNA, and we might expect an enhancement of the band-like behavior. Instead, our results reveal a different mechanism. For both filled and empty G4 columns, we find that the inter-plane π superposition is not sufficient to induce the formation of delocalized orbitals along the axis of the *quadruplex*: The right panel in Figure 2 shows that the bands of the 3G4/ K^+ column are flat, typical of supramolecular systems in which the orbitals remain localized at the molecules. The bandstructure identifies the presence of band-multiplets, each constituted of 12 energy levels. The 12 electron orbitals associated to a multiplet have identical character and localize on the 12 guanines in the unit cell. The energy levels in a multiplet are separated by an average energy difference of 0.02 eV, smaller than the room-temperature energy $k_B T$: therefore, the coupling with the thermal bath allows the G-localized neighboring orbitals of a multiplet to interact, producing an effective delocalized orbital. The resulting DOS (Fig. 2), obtained with a gaussian broadening to the calculated one-electron energy eigenvalues, shows filled and empty effective bands, separated by a gap of 3.3 eV and 3.5 eV for the 3G4 and the 3G4/ K^+ tubes, respectively. Each of the five peaks labeled with letters in Figure 2 takes origin from

one G orbital: For instance, peak **a** is the convolution of the π -like HOMO's of the 12 unit guanines. The amplitude of this peak is 0.3 eV for both wires. The only meaningful difference that we note between 3G4 and 3G4/K⁺ is a downward shift of the σ -like peak **b** in 3G4/K⁺. By a comparative analysis of a similar shift for σ -like orbitals of the G-ribbons [11], resulting upon the introduction of electrostatic interactions, we attribute the downward shift of the σ -like peak **b** in the 3G4/K⁺ tubes to the electrostatic attractive interaction induced by the inclusion of the K⁺ ions.

We show in Figure 3 contour plots of the HOMO convolution (peak **a** of the DOS) of 3G4/K⁺ in a plane containing (top) and perpendicular to (bottom) the axis of the quadruple helix. The side-view contour plot shows the formation of an extended orbital in the outer side of the nucleobase stack, due to C-N bonds, that constitutes a channel for electron mobility along the helical axis. The contour plots also reveal that the K species is fully ionized, and therefore the inner cavity of the column is free of charge. Thus, conductivity in the G-wires may not be attributed to metallic bonds between the K atoms, neither to their ionic motion, because of the high stability of the structure.

By means of first-principle calculations, we have demonstrated the stability of columnar structures based on guanine stacks, in the abundance of K⁺ ions. The π - π coupling does not induce extended states and dispersive energy bands. However, the energy separation between neighboring localized states is so small that coupling can be easily induced, e.g., by room-temperature thermal hopping. Therefore, 3G4/K⁺ tubes under suitable conditions, are expected to exhibit an effective behavior of wide-bandgap semiconductors. This feature, along with the possibility of forming extended stacked wires at the nanoscale length, makes them appealing for the development of biomolecular electronics.

This work was supported by INFN through *Progetto Calcolo Parallelo*, and PRA-SINPROT.

-
- [1] G. Gottarelli, G. P. Spada, and A. Garbesi, in "Comprehensive Supramolecular Chemistry", volume 9, edited by J. L. Atwood, J. E. D. Davies, D. D. MacNicol, and F. Vögtle, Pergamon, 1996.
 - [2] G. Gottarelli, S. Masiero, E. Mezzina, G. P. Spada, P. Mariani, and M. Recanatini, *Helv.*

- Chimica Acta* **81**, 2078 (1998).
- [3] M. Bixon, B. Giese, S. Wessely, T. Langenbacher, M. E. Michel-Beyerles and J. Jortner, *Proc. Nat. Acad. Sci. USA* **96**, 11713 (1999).
 - [4] T. C. Marsh, J. Vesenska, and E. Enderson, *Nucleic Acids Res.* **23**, 696 (1995).
 - [5] K. Phillips, Z. Dauter, A. I. H. Murchie, D. M. J. Lilley, and B. Luisi, *J. Mol. Biol.* **273**, 171 (1997). X-ray structure: NDB ID UDF062.
 - [6] S. L. Forman, J. C. Fettingner, S. Pieraccini, G. Gottarelli, and J. T. Davis, *J. Am. Chem. Soc.* **122**, 4060 (2000).
 - [7] C. Joachim, J. K. Gimzewski, and A. Aviram, *Nature* **408**, 541 (2000).
 - [8] D. Porath, A. Bezryadin, S. de Vries and C. Dekker, *Nature* **403**, 635 (2000).
 - [9] R. Rinaldi, E. Branca, R. Cingolani, S. Masiero, G. P. Spada, and G. Gottarelli, *Appl. Phys. Lett.* **78**, 3541 (2001).
 - [10] G. B. Schuster, *Acc. Chem. Res.* **33**, 253 (2000).
 - [11] A. Calzolari, R. Di Felice, E. Molinari, and A. Garbesi, *Phys. Rev. B*, in press; and *Physica E*, in press.
 - [12] M. Bockstedte, A. Kley, J. Neugebauer, and M. Scheffler, *Comp. Phys. Comm.* **107**, 187 (1997).
 - [13] R. M. Dreizler and E. K. U. Gross, *Density Functional Theory. An Approach to the quantum many-body problem.*, Springer-Verlag, Berlin, 1990.
 - [14] A. D. Becke, *Phys. Rev. A* **38**, 3098 (1988); C. Lee, W. Yang, and R. C. Parr, *Phys. Rev. B* **37**, 785 (1988).
 - [15] M. Bernasconi, P. L. Silvestrelli, and M. Parrinello, *Phys. Rev. Lett.* **81**, 1235 (1998).
 - [16] Y. Ye, R. S. Chen, A. Martinez, P. Otto, and J. Ladik, *Sol. St. Commun.* **112**, 139 (1999).
 - [17] The *quadruplexes* characterized by X-ray contained Na^+ ions rather than K^+ ions: we assumed the same starting positions for the K^+ ions.
 - [18] C. G. Van de Walle, D. B. Laks, G. F. Neumark, and S. T. Pantelides, *Phys. Rev. B* **47**, 9425 (1993).
 - [19] Along the axis of a *G-quadruplex*, the potassium ions are separated by a distance of 3.4 Å, smaller than the interatomic distance in the bulk *fcc* metal.
 - [20] J. Gu and J. Leszczynski, *J. Phys. Chem. A* **104**, 6308 (2000).

FIG. 1: (a) Schematic representation of the planar G4; (b) G-wire: side view of the three repeated tetramers in presence of K^+ ions; (c) schematic top view of the stacked G4's in the helical wire; (d) relative formation energy vs. Fermi level, $\Delta E^{form}=0$ corresponds to the chemical potential of the single guanine, $E_F=0$ marks the top of the valence band.

FIG. 2: The left panel illustrates the DOS of the periodic G4 stacks with (bottom) and without (top) K^+ ions. The right panel shows the almost dispersionless energy levels of the $3G4/K^+$ system. Γ (A) is the center (edge) of the 1D Brillouin Zone in the stacking direction. Peaks in the DOS are labeled to identify their common microscopic origin.

FIG. 3: Contour plots of the symmetrized charge density of the HOMO in two different planes containing (top) and cutting (bottom) the axis of the G4 stack. Top: the vertical direction coincides with the axis of the stack, the horizontal direction is perpendicular to such axis and goes through the atoms labeled in the figure. Bottom: the fixed-density contours are shown in the plane containing the middle G4 assembly of Fig. 1b.

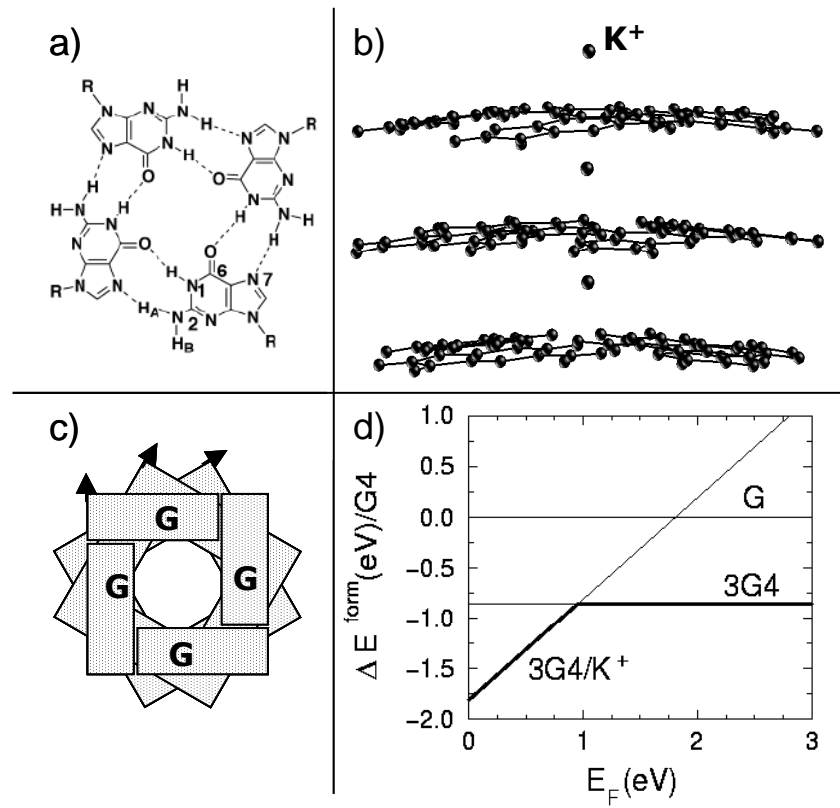


Fig. 1

A. Calzolari et al.
Appl. Phys. Lett. (2002), in press.

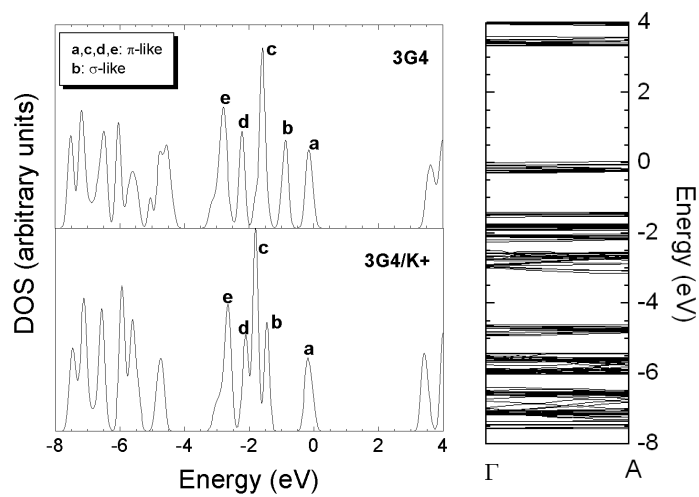


Fig. 2

A. Calzolari et al.
Appl. Phys. Lett. (2002), in press.

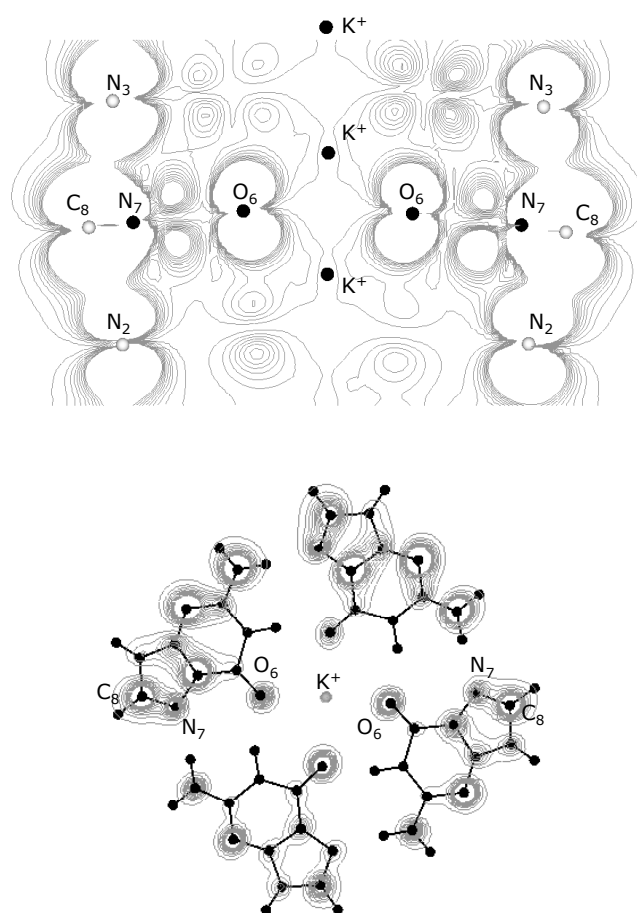


Fig. 3

A. Calzolari et al.
Appl. Phys. Lett. (2002), in press.